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PREDICTING THE SEVERITY OF THE COURSE AND OUTCOMES OF VIRAL ENCEPHALITIS USING MULTIVARIATE MATHEMATICAL ANALYSIS

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Abstract:
The relevance of the subject under study lies in the wide distribution, severity of the course, and the frequency of disabling consequences of inflammatory diseases of the central nervous system, which determines the importance of predicting their course and outcome, as the principal component of the diagnostic process. The main purpose of this study was to develop a predictive model of the severity of inflammatory diseases of the central nervous system, using methods of multifactorial mathematical analysis. The basis of the methodological approach in this study was an experimental, practical study of the principles of creating a model based on mathematical analysis methods for predicting the severity of the course and consequences of viral encephalitis. In this paper, results were obtained indicating the effectiveness of the proposed method for predicting and evaluating the course of viral encephalitis in patients of the groups taken for study. Negative results in predicting negative outcomes of this disease according to the proposed method amounted to only 6.7% (6 patients out of 90), while errors in predicting positive outcomes were noted at the level of 5.6% (5 patients out of 90). According to the results of the prognosis, all patients who took part in the examination underwent therapy correction. The duration of administration of neurometabolic drugs was also increased, due to the processing of the results of a multifactorial mathematical analysis. The practical significance of the results obtained in this study lies in the possibility of their implementation in the practice of medical institutions of various profiles to compile predictive models of the course and outcome of inflammatory diseases of the central nervous system.

Keywords: Virus, predictive models, medical sciences, calculated parameters, pathogens, diagnostics of diseases

1. INTRODUCTION

The problem of this study is that acute viral encephalitis, due to its disabling nature and severe neurological deficit in patients, is still an important problem today. In medical practice, those methods of forming predictions of the severity of the course and outcome of viral encephalitis were previously used, which were based on a comprehensive assessment of clinical and neurological disorders, as well as identified functional problems in this disease (Kepa et al., 2006). Therewith, these violations were determined by using electroencephalography (EEG) methods. The key disadvantage of this method is its low sensitivity in viral encephalitis, reaching only 45%. Therewith, during the acute course of this disease, the nature of changes in electroencephalography indicators may be non-specific or not manifest at all, which does not give reliable grounds to consider this method of forecasting objective. This determines the relevance of the development and implementation of other mathematical methods for predicting the course and outcomes of viral encephalitis. The developed and presented prognostic model for predicting the course and outcomes of acute viral encephalitis based on multifactorial mathematical and statistical processing is of immense importance for the timely diagnosis and correction of treatment of this disease. Its practical implementation opens more opportunities to improve the effectiveness of the diagnosis of viral diseases of the central nervous system and contributes to an increase in the number of cases of a favourable outcome of treatment.

M.A. Hansen et al. (2020) conducted an experimental study of risk factors and outcome of viral encephalitis in elderly patients. Scientists have found that it is not possible to establish the aetiology of encephalitis and predict a favourable clinical outcome in most elderly patients. Among the unfavourable prognostic factors, they distinguish the age of patients over 65 years, the presence of seizures, and an average score on the coma scale of less than 13 units.

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T. Pichl et al. (2022) in a joint study aimed at investigating the results of brain imaging in neurological infection with encephalitis virus note that this method allows obtaining essential information about the aetiology of infectious encephalitis. According to scientists, the use of mathematical modelling of the severity of the disease provides data on the nature of brain damage, which is necessary to prescribe efficacious treatment.

K-V. Liang and T-K. Chen (2022) conducted a joint scientific study of anti-NMDA receptor encephalitis manifested by fever with an unknown cause, during which it was noted that viral encephalitis can cause difficulties for non-psychiatric or neurological specialists in diagnosis and subsequent treatment. This makes it expedient to use the method of mathematical analysis to compare the factors determining the effectiveness of diagnosing the disease and further tracking the course of treatment.

D. Glavin et al. (2021) conducted a scientific study of several problematic aspects of the aetiology of COVID-19 viral encephalitis with SARS-CoV-2 detected in cerebrospinal fluid simulating a stroke. In their study, scientists note that there are difficulties associated with the diagnosis of neurological pathology during the COVID-19 coronavirus pandemic, which causes clinical consequences (Glavin et al., 2021). The situation can be optimally resolved through the introduction of mathematical analysis methods that factor in many aspects that affect the accuracy of diagnosis and prediction of the nature of the course of the disease.

H.U. Berdieva (2014), in her study of the features of the course of viral encephalitis and meningoencephalitis in children, notes that such diseases occur with inflammation of the membranes of the brain and its substance. Therewith, it is in children that viral encephalitis is characterized by a prominent degree of involvement of the medulla and meninges in the pathology.

The main purpose of this study was to create a mathematical model that allows predicting the severity of viral encephalitis, as well as all possible outcomes of the disease.

2. MATERIALS AND METHODS

The methodological framework of this paper is an experimental study of the sequence of application of mathematical analysis methods, considering a significant number of factors for the development and practical application of predictive models of the course and consequences of inflammatory viral diseases of the central nervous system. The theoretical framework of the study included the analysis of the results of scientific studies of domestic and foreign scientists who investigated the complex of problematic aspects of constructing mathematical models for predicting the nature of the course of viral diseases of the central nervous system.

A method of forming models of prognoses and consequences of the course of inflammatory diseases of the central nervous system in general and viral encephalitis in particular was proposed. The presented methodology was based on a comprehensive assessment of disorders, namely clinical, neurological, neuroimmune, and neuroimaging ones. This allowed for prompt correction of therapeutic procedures prescribed to patients, as well as a significant reduction in the intensity of residual changes in the central nervous system (Walti et al., 2018).

During the study, 58 patients aged 18-70 years with viral encephalitis were examined, clinical neurological, neuroimmunological, and neuroimaging studies were conducted. The study was conducted at the Department of Neurology of the Andijan State Medical Institute (Uzbekistan). The group of patients under study was evenly distributed by gender, it included individuals with mild, moderate, and severe forms of the disease. To form predictive models, the method of logistic regression was applied, which allowed accurately determining the severity of the disease in individual groups of patients. This allowed developing a predictive model that determined the probability of occurrence of various scenarios of the course of the disease and determining the boundary regression indicators of viral encephalitis.

Based on the obtained indicators for assessing the regression of viral encephalitis, a mathematical model was developed to calculate the nature of the course of viral encephalitis in patients in a state of varying severity. The following formulas were used in this mathematical model.

The probability of a mild course of encephalitis disease (1):

$$P_{\%}(M) = 1/(1+e^{z}) \times 100\%; z = -2.08 + 22.01 \times X_{\text{CSF protein}} + 0.72 \times X_{\text{large CICs}} + 0.34 \times X_{\text{CSF cytosis}} + 0.28 \times X_{\text{CRP}} + 0.12 \times X_{\text{smal CICs}} - 0.25 \times X_{\text{TNF}\alpha} - 0.35 \times X_{\text{age}} - 3.6 \times X_{\text{CSF-P}} - 4.64 \times X_{\text{IL-1}\beta}.$$

(1)

The probability of moderate severity of viral encephalitis (2-3):

$$P_{\%}(M-MS) = 1/(1+e^{z}) \times 100\%; z = -17.15 + 22.01 \times X_{\text{CSF protein}} + 0.72 \times X_{\text{large CICs}} + 0.34 \times X_{\text{CSF cytosis}} + 0.28 \times X_{\text{CRP}} + 0.12 \times X_{\text{smal CICs}} - 0.25 \times X_{\text{TNF}\alpha} - 0.35 \times X_{\text{age}} - 3.6 \times X_{\text{CSP-P}} - 4.64 \times X_{\text{IL-1}\beta},$$

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(2)

$$P_{\%}(M-S) = P_{\%}(M-MS) - P_{\%}(M).$$

(3)

The probability of a severe form of viral encephalitis (4-5):

$$P_{\%}(M-S) = 1/(1+e^{z}) \times 100\%; z = -32.56 + 22.01 \times X_{CSF\ protein} + 0.72 \times X_{large\ CICs} + 0.34 \times X_{CSF\ cytosis} + 0.28 \times X_{CRP} + 0.12 \times X_{smal\ CICs} - 0.25 \times X_{TNF\alpha} - 0.35 \times X_{age} - 3.6 \times X_{CSP-P} - 4.64 \times X_{IL-1\beta},$$

(4)

$$P_{\%}(S) = P_{\%}(M-S) - P_{\%}(M-MS).$$

(5)

The probability of an extremely severe form of viral encephalitis (6):

$$P_{\%}(ES) = 100\% - P_{\%}(M-S). \quad (6)$$

Through the application of binary logistic regression methods, a predictive model was developed (7):

$$P = 1/(1+e^{z}); z = 5.808 \times X_{IL-1\beta} + 6.529 \times X_{TNF\alpha} + 4.713 \times X_{CSF\ protein} + 7.587 \times X_{CSF\ cytosis} + 5.031 \times X_{CRP} + 4.650 \times X_{ICHMRI} + 1.1179. \quad (7)$$

where P is the probability of death in encephalitis (in fractions of one), $X_{IL-1ß}$ is an elevated level of IL-1ß, pg/ml, $X_{TNFα}$ is an increased level of TNFα, pg/ml, $X_{CSF\ protein}$ is the presence of protein in CSF, g/l, $X_{CSF\ cytosis}$ is the elevated cytosis level in CSF, µl, X_{CRP} is the elevated level of C-reactive protein, mg/l, X_{ICHMRI} is the presence of infiltration in the cerebral hemispheres in MRI (0 – absence, 1 – presence).

3. RESULTS

The relevance of the neurological problems of inflammatory diseases of the central nervous system (CNS) is conditioned upon their significant spread, the severity of the course, as well as the high incidence of disability, which reaches 60% (Hansen et al., 2020). Making reliable forecasts of the course of these diseases and their outcomes is one of the key issues of diagnosis at early stages. Correct diagnosis allows prescribing the necessary therapeutic procedures promptly, as well as adjusting the course of the treatment if necessary. This allows avoiding the severe course of inflammatory diseases and substantially reduces the probability of disabling consequences in patients.

There is a way to create predictive models of the course and outcomes of tick-borne viral encephalitis, which is based on assessing the level of neurological disorders, parameters of stem acoustic potentials. It is based on the fact that viral tick-borne encephalitis is a vector-borne disease caused by the tick-borne encephalitis virus and spreads quite quickly through the bites of Ixodes ricinus ticks infected with this virus (Parfut et al., 2023). The common subtype of encephalitic tick in Europe (TBEV-Eu) is dangerous as a potential causative agent of the epidemic in 27 European countries. This fact carries a substantial danger for the population, since the risk of infection with viral encephalitis and the rapid spread of the epidemic increases, which can lead to unpredictable consequences. Earlier studies have indicated a number of various risk factors for all causes of encephalitis (Thakur et al., 2013). However, prognostic models were created only for particular aetiologies of encephalitis (Qiu et al., 2019). They did not cover all possible scenarios of the course of this disease, including various stages, from mild to severe.

Considering the above information, a new way of forming models of prognoses and outcomes of inflammatory diseases of the central nervous system was proposed. This method is based on a comprehensive assessment of clinical, neurological, neuroimmune, and neuroimaging disorders. This allows promptly correcting the course of treatment of patients, as well as achieving a considerable reduction in the frequency of residual changes in the central nervous system (Soung et al., 2022). Using the method of ordinal logistic regression, prognostic models were obtained that allow determining the probability of the course (mild, moderate, severe, extremely severe) of encephalitis disease, proceeding from clinical neurological data (age, gender, plegia (paresis), paraanesthesia, tetraanesthesia, pathological reflexes, trophic changes, etc.), neuroimaging data (MRI of the brain and spinal cord) and neuroimmune data (TNFα, IL-1β, IL-6, CICs, CSF, CRP).

At the next stage, a predictive model was developed that determines the probability of encephalitis (Table 1).

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Table 1. Evaluation of encephalitis factors

Seq. No.	Factor	Grade	95% CI	P
1	Presence of protein in CSF, g/l	22.01	-224.03; 268.04	0.031*
2	Elevated level of IL-6, pg/ml	2.52	-17.35; 22.39	0.062
3	Elevated level of large cics in the blood, IU/ml	0.72	-12.03; 13.47	0.012*
4	Elevated cytosis level in CSF, mcl	0.34	-10.75; 11.41	0.003*
5	Elevated level of C-reactive protein, mg/l	0.28	-18.69; 18.13	0.001*
6	Elevated level of small cics in the blood, IU/ml	0.12	-10.97; 11.21	<0.001*
7	Elevated tnfα level, pg/ml	-0.25	-59.07; 58.57	<0.001*
8	Age, year	-0.35	-20.29; 19.59	0.001*
9	Pandy's positive reaction in CSF, g/l	-3.6	-60.69; 53.75	0.015*
10	Elevated levels of IL-1ß, pg/ml	-4.64	-80.67; 71.39	0.014*

Note: * – differences in indicators are statistically significant ($p<0.05$).

Source: compiled by the author.

Figure 1 shows the number of patients with various degrees of severity of encephalitis.

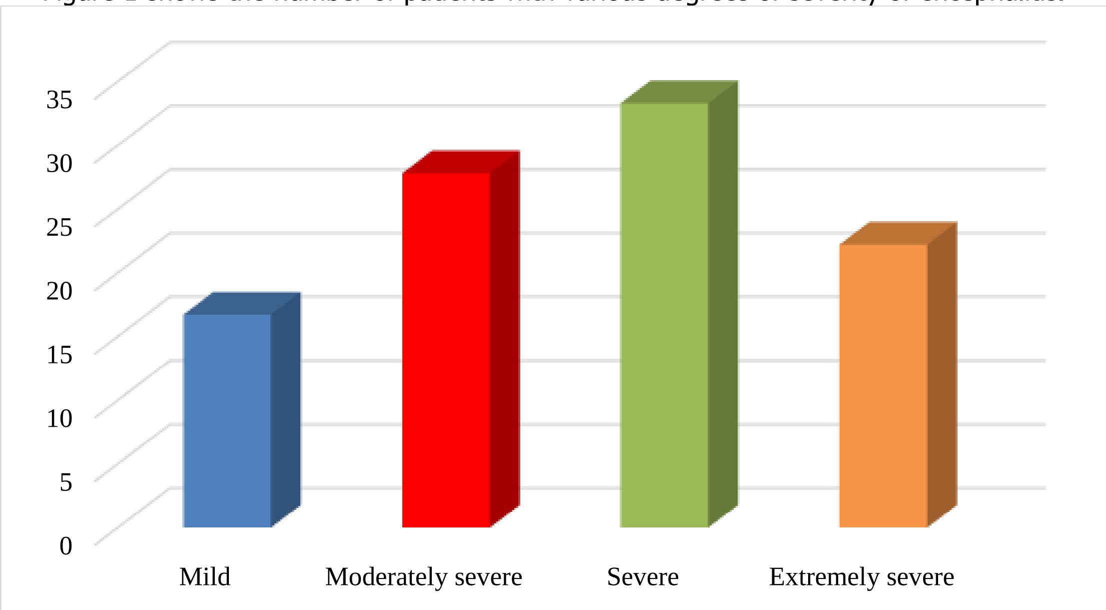

Figure 1. The total number of patients with various degrees of severity of viral encephalitis.

Source: compiled by the author.

Table 2 shows the boundary indicators of disease regression estimation for the selected variable parameter.

Table 2. Boundary indicators for assessing the regression of viral encephalitis

Variable indicator	Value
Mild	2.08
Mild – Moderate	17.15
Mild – Severe	32.56

Source: compiled by the author.

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Based on the indicators presented in Table 2, a calculation scheme was developed to determine the scenarios of viral encephalitis of varying severity.

The probability of a mild course of encephalitis disease can be calculated as follows (8):

$$P_{\%}(M) = 1/(1+e^{z}) \times 100\%; z = -2.08 + 22.01 \times X_{CSF\ protein} + 0.72 \times X_{large\ CICs} + 0.34 \times X_{CSF\ cytosis} + 0.28 \times X_{CRP} + 0.12 \times X_{smal\ CICs} - 0.25 \times X_{TNF\alpha} - 0.35 \times X_{age} - 3.6 \times X_{CSP-P} - 4.64 \times X_{IL-1\beta}. \quad (8)$$

The probability of a moderately severe course of encephalitis disease can be calculated as follows (9-10):

$$P_{\%}(M-S) = 1/(1+e^{z}) \times 100\%; z = -17.15 + 22.01 \times X_{CSF\ protein} + 0.72 \times X_{large\ CICs} + 0.34 \times X_{CSF\ cytosis} + 0.28 \times X_{CRP} + 0.12 \times X_{smal\ CICs} - 0.25 \times X_{TNF\alpha} - 0.35 \times X_{age} - 3.6 \times X_{CSP-P} - 4.64 \times X_{IL-1\beta}, \quad (9)$$

$$P_{\%}(MS) = P_{\%}(M-MS) - P_{\%}(M). \quad (10)$$

The probability of a severe course of encephalitis disease can be calculated as follows (11-12):

$$P_{\%}(M-S) = 1/(1+e^{z}) \times 100\%; z = -32.56 + 22.01 \times X_{CSF\ protein} + 0.72 \times X_{large\ CICs} + 0.34 \times X_{CSF\ cytosis} + 0.28 \times X_{CRP} + 0.12 \times X_{smal\ CICs} - 0.25 \times X_{TNF\alpha} - 0.35 \times X_{age} - 3.6 \times X_{CSP-P} - 4.64 \times X_{IL-1\beta}, \quad (11)$$

$$P_{\%}(S) = P_{\%}(M-S) - P_{\%}(M-MS). \quad (12)$$

The probability of an extremely severe course of encephalitis disease can be calculated as follows (13):

$$P_{\%}(ES) = 100\% - P_{\%}(M-S). \quad (13)$$

The significance of the impact of the selected factor variables in improving forecasts, which are formed through a mathematical model, was assessed through the difference of negative indicators of the doubled logarithm of the probability function (-2_{LL}). This parameter was determined before the start of factor accounting ($-2_{LL}=48.78$) and after the start of accounting ($-2_{LL}<0.001$), which equates to the parameter $\chi^2=48.78$ and indicates a statistically significant improvement in the accuracy of forecasts ($p<0.001$).

Figure 2 shows a comparison of the course of encephalitis in patients depending on indicators of statistical significance.

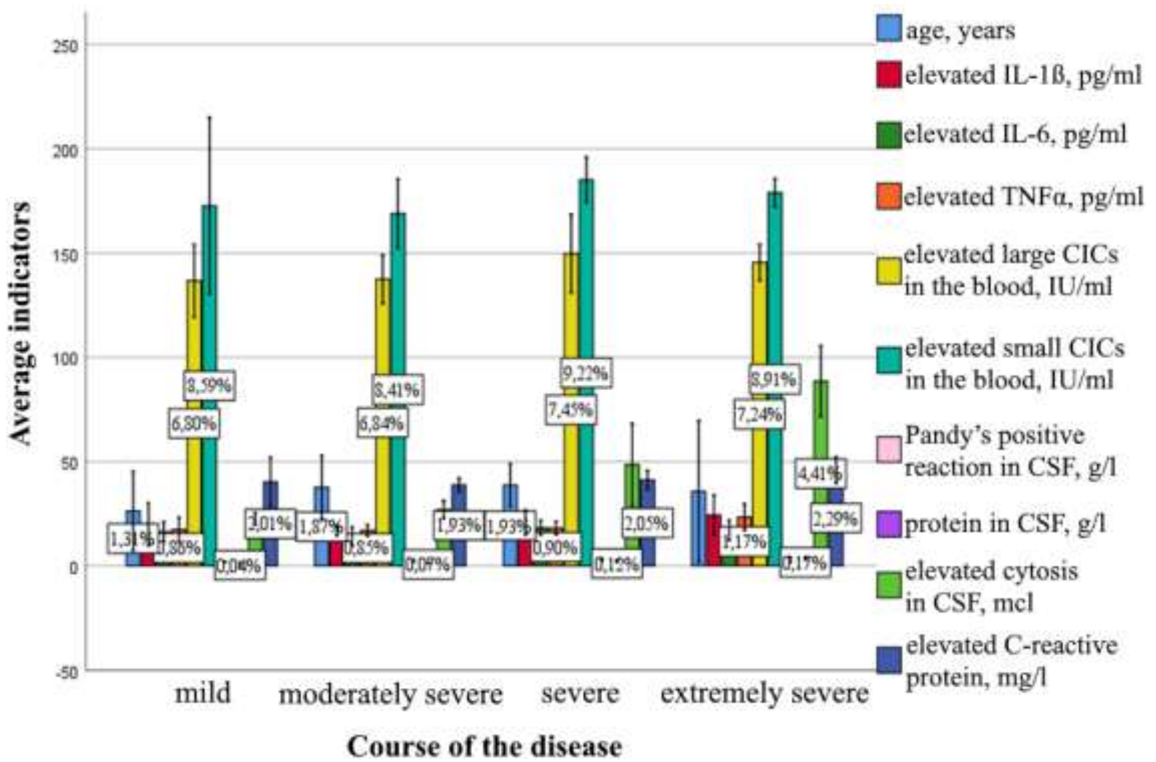

Figure 2. Comparison of the course of encephalitis in patients depending on statistically significant indicators

Source: compiled by the author.

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A consistent comparison of the planned and real repetition frequencies of particular parameters of the dependent variable, carried out by using the Pearson agreement indicator, allowed determining a significant indicator of comparison and difference of frequencies p=1.

Considering the value of the pseudo-R^2 parameter, Nigelkirk, the factors included in this mathematical model were determined by 100% of the variance of the dependent variable. Using the Pearson rank correlation method, a statistically significant correlation was established between the expected and observed values of the severity of myelitis (p=1.00; p<0.001). The sensitivity of the developed model in forecasting was 100%.

To solve the problem of predicting the outcome of the disease of myelitis, encephalitis and encephalomyelitis, the method of binary logistic regression was applied. Clinical and neurological and neuroimmune indicators were considered during the development. The outcome of encephalitis disease was statistically processed, and the following values were revealed (Table 3).

Table 3. Statistical analysis of predicting the outcome of encephalitis disease

Predictors	Regression coefficients (b)	Statistical significance (p)
Age, year	0.201	0.654
Gender (f, m)	1.639	0.200
Presence of hemiparesis, hemiplegia	0.018	0.893
Presence of monoparesis, monoplegia	0.195	0.659
Presence of hemianesthesia	0.565	0.452
Presence of monoanesthesia	0.195	0.659
Presence of hyperreflexia	0.006	0.937
Presence of extrapyramidal disorders	3.453	0.063
Violation of coordination movements	0.049	0.825
Presence of meningeal symptoms	0.327	0.567
Damage of the III pair of craniocerebral insufficiency	1.121	0.290
Damage of the IV pair of craniocerebral insufficiency	0.327	0.567
Peripheral damage of the VII pair	0.327	0.567
Central damage of the VII pair	2.179	0.140
Presence of tongue deviation	2.179	0.140
Presence of bulbar paralysis	2.471	0.116
Presence of convulsive syndrome	1.639	0.200
Consciousness (sopor, coma)	1.022	0.312
Elevated levels of IL-1ß, pg/ml	5.808	0.016*
Elevated level of IL-6, pg/ml	0.239	0.625
Elevated tnfα level, pg/ml	6.529	0.011*
Elevated level of large cics in the blood, IU/ml	0.044	0.835
Elevated level of small cics in the blood, IU/ml	0.530	0.467
Presence of protein in CSF, g/l	4.713	0.030*
Elevated cytosis level in CSF, mcl	7.587	0.006*
Increased level of C-reactive protein, mg/l	5.031	0.025*
Presence of infiltration of the large hemispheres in MRI	4.650	0.031*
Presence of cerebellar infiltration in MRI	1.609	0.205
Presence of brain stem infiltration in MRI	1.068	0.301
Presence of retinal angiopathy in the HD	0.565	0.452
Presence of oedema, shading of the optic disc in the HD	1.639	0.200

Note: * – changes in the indicator are statistically significant (p<0.05).
Source: compiled by the author.

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Figure 3 shows data comparing the outcome of encephalitis in patients depending on statistically significant indicators.

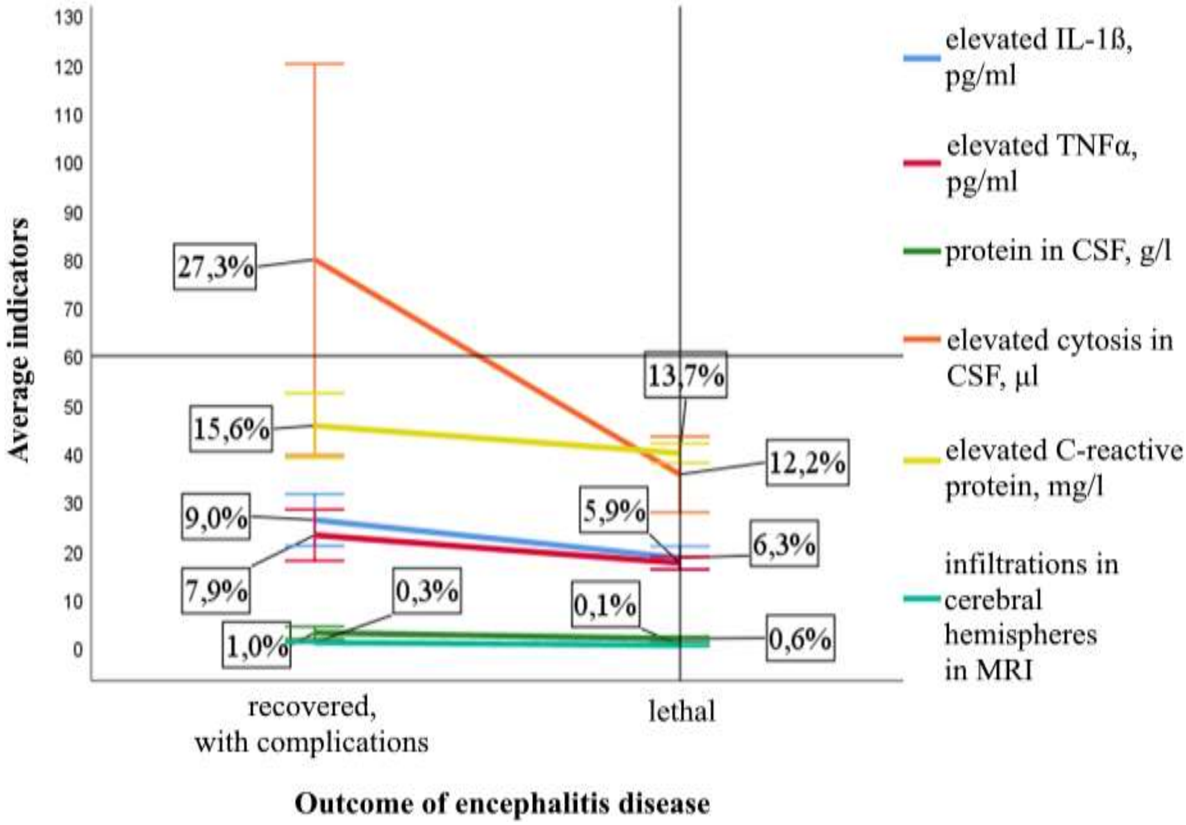

Figure 3. Comparison of the outcome of encephalitis in patients depending on statistically significant indicators

Source: compiled by the author.

Using the binary logistic regression method, the following predictive model was developed (14):

$$P = 1/(1 + e^{z}); z = 5.808 \times X_{IL-1\beta} + 6.529 \times X_{TNF\alpha} + 4.713 \times X_{CSF\ protein} + 7.587 \times X_{CSF\ cytosis} + 5.301 \times X_{CRP} + 4.650 \times X_{ICHMRI} + 1.179. \quad (14)$$

Based on the indicated parameters of the regression coefficients, a direct relationship is found between such factors as an elevated level of IL-1β, an elevated level of TNFα, the presence of protein in the CSF, an elevated level of cytosis in the CSF, an elevated level of C-reactive protein, the presence of infiltration in the cerebral hemispheres in MRI with the fatal outcome of encephalitis. The mathematical model obtained as a result of (14) was statistically significant ($p<0.001$).

The boundary parameter of the function P was fixed at 0.5. Consequently, when the parameter P reached more than 0.5, the probability of a fatal outcome of encephalitis was considered significant, and with parameters below 0.5, the probability of a fatal outcome of encephalitis was considered small. With the established boundary parameter, the sensitivity of the mathematical model was noted at the level of 75.0%, specificity – 92.9%.

The effectiveness of the proposed method for predicting the course and outcomes of inflammatory diseases of the central nervous system was evaluated in 90 patients in the age range from 18 to 70 years who were patients of the clinic of neurological diseases. False negative parameters in the formation of negative forecasts of encephalitis according to this formula were recorded at merely 6.7% (6 examined patients out of 90), the level of error in the forecasts of successful outcomes was noted at 5.6% (5 examined patients out of 90).

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After the prognostic data on the nature of the course and the probable outcome of the disease were obtained, all patients underwent correction of neurometabolic, antiviral, anti-inflammatory, and antibacterial therapy. If a negative outcome of inflammatory diseases of the central nervous system was recognized as the most probable, the total duration of parenteral administration of neurometabolic drugs increased to at least 3 weeks with further use of drugs for a period from 4 to 6 weeks. If a positive outcome of inflammatory diseases of the central nervous system was predicted, neurometabolic drugs were administered directly inside for at least 40 days. Reducing the total duration of parenteral administration of drugs allowed substantially extending the neurometabolic therapy in outpatient settings, which considerably reduced the time of therapy of patients in a hospital setting, at least up to 20 days.

4. DISCUSSION

D.A. Brown et al. (2018), in their study aimed at investigating problematic issues of diagnosis and treatment of viral encephalitis, pay attention to the fact that viral encephalitis is one of the causes of disorders of motor activity in adults. This necessitates the development and implementation of an effective mathematical model for predicting the severity of viral encephalitis. It is also noted that patients diagnosed with viral encephalitis pose a substantial diagnostic problem, since some of them respond to immunosuppression, while requiring intensive treatment (Brown et al., 2018). The conclusions of scientists fundamentally correspond to the results of the present study, while scientists focus on the complexity of the diagnosis of viral encephalitis, in the context of the importance of the correct appointment of subsequent therapy.

D. Ruzek et al. (2020) conducted a scientific study of the specific features of the spread of viral and tick-borne encephalitis in Russia and Europe. Scientists note that viral encephalitis caused by bites of encephalitic ticks is characterized by severe fever, but it can cause aggressive neurological manifestations. According to the researchers, the use of multifactorial mathematical analysis methods to predict the severity of the course and results of viral encephalitis therapy has substantial prospects for use in the practice of medical institutions (Ruzek et al., 2020). The conclusions of the researchers coincide with the results obtained in the present study, while the assessment of the prospects for the consequences of this disease in case of incorrect prediction of its course deserves attention.

At the same time, K. Kong et al. (2015) in a joint study considered certain epidemiological features of viral encephalitis in the context of the use of special diagnostic methods and treatment. According to scientists, the use of an accurate and highly sensitive method of testing the virus that causes encephalitis is an effective method of predicting the severity of this disease. This study notes that the practical application of the multiplex RT-PCR system allows for effective diagnosis of viral encephalitis and largely influences the choice of therapy measures, which is vital from the standpoint of predicting the outcome of the disease (Kong et al., 2015). The researchers' conclusions correspond to the results that were obtained in this study, while highlighting the importance of using the method of testing the virus that causes encephalitis.

The subject under study was partly further developed in a joint study by Y. Kobayashi et al. (2022), who examined problematic aspects of the development of viral encephalitis that followed vaccination against the COVID-19 virus. In this scientific study, it was noted that viral encephalitis should be considered one of the side effects of the COVID-19 coronavirus disease, which is associated with a weakening of the immune protection of the human body and the negative consequences of vaccination. According to scientists, the manifestation of symptoms of viral encephalitis after vaccination requires detailed investigation using mathematical analysis methods to organize data (Kobayashi et al., 2022). The researchers' conclusions do not fundamentally contradict the results of the present study, while their opinion regarding the perception of viral encephalitis as a side effect of coronavirus is controversial and requires verification.

Y. Tsuruyama et al. (2020) conducted a joint scientific study of a clinical case of viral encephalitis in a young patient. Scientists pay attention to the fact that cases of complications for the central nervous system due to exposure to the encephalitis virus are quite common. Therewith, the nature of these complications varies depending on the nature of the course of the disease, which makes it expedient to develop and implement a comprehensive mathematical model describing the relative severity of the course of the disease in each case and possible outcome options (Tsuruyama et al., 2020). The results obtained by scientists fundamentally coincide with the results of the present study, while their conclusion regarding the frequency of complications for the central nervous system due to viral encephalitis is controversial.

D. Ruzhek, G. Dobler and O. D. Mantke (2010), in a joint scientific study of the pathogenesis and clinical course of tick-borne viral encephalitis, address the fact that this disease belongs to the number of severe neurological diseases that have spread over vast territories of Europe and northern Asia. Therewith, clinical symptoms in the form of fever develop only in some infected people, but in each case severe consequences are possible, up to a chronic course and a fatal outcome (Ruzek et al., 2010). The use of multifactorial mathematical analysis in the practice of medical institutions at any stage of the course of the disease will help get an objective picture of all changes and predict the possible outcome in each case. The opinion of the researchers does not contradict the results of the present study, a remark about the degree of spread of viral encephalitis in particular geographical regions deserves special attention.

E. Petri, D. Gniel, and O. Zent (2010) in a joint scientific study aimed at investigating the key trends of tick-borne viral encephalitis in epidemiology, as well as the general principles of the treatment used, pay attention to the fact that this disease is among the international health problems, since there is a tendency to increase the number of risk zones and registered foci diseases in various parts of the world. According to scientists, with relative fluctuations in the total number of cases of detection of this disease, the presence of severe health consequences should be considered, which necessitates the expansion of the range of mathematical models that track the nature of the course of the disease and predict the outcome (Petri et al., 2010). The conclusions of the researchers are fully consistent with the results of the present study, while opening more research prospects in the field of analysing potential risk areas for viral encephalitis and preventing its spread.

At the same time, A. Piantodosi and I.H. Solomon (2022) in a joint scientific work investigated problematic aspects of the diagnosis of the Powassan virus, which causes a severe form of encephalitis. Scientists note that despite the relative knowledge of this virus, there are numerous negative consequences of the course of the disease with viral encephalitis, which it causes. The use of the binary logistic regression method in predicting the outcome of viral encephalitis caused by this virus has shown considerable effectiveness, which determines the expediency of using this technique in the future (Piantadossi and Solomon, 2022). The opinion of the researchers fundamentally corresponds to the results obtained in the present study, in terms of the evaluation of the effectiveness of the applied methods of mathematical modelling.

K. Messacar et al. (2018) jointly investigated problematic aspects of the treatment of viral encephalitis in children in the United States. Therewith, scientists note that viral encephalitis means inflammation of the parenchyma of the brain, which is a state of serious neurological dysfunction. The researchers concluded that there is a wide variety of infectious and non-infectious aetiology associated with encephalitis, and the cause of the disease in some cases is still unclear, even with extensive testing (Messacar et al., 2018). The solution can be found in the introduction of methods of mathematical data processing, which allow diagnosing the disease and qualitatively predict the nature of its course in most cases. The researchers' conclusions are fully correlated with the results of the present study, additionally highlighting some problematic aspects of the aetiology of viral encephalitis.

Thus, the discussion of the results of the present study in the context of their analytical comparison with the results of other studies on some related topics showed their fundamental correspondence in some key aspects. This is evidence of the scientific reliability of the results obtained in this scientific work, as well as the expediency of their subsequent use in the practical plane, with the direct introduction of methods of multifactorial mathematical analysis to predict the severity of the course and outcome of viral encephalitis in medical institutions.

5. CONCLUSIONS

The developed multifactorial mathematical model for predicting the severity of the course and outcome of inflammatory diseases of the CNS, composed of clinical neurological (age, gender, plegia (paresis), paraanesthesia, tetraanesthesia, pathological reflexes, trophic changes, etc.), neuroimaging (MRI imaging of the brain and spinal cord) and neuroimmune (TNFα, IL-1β, IL-6, CEC, CSF, CRP) data showed high predictive value before and after their application in clinical practice. The use of these prognostic models in clinical practice on a large scale can prevent the severe course and adverse outcomes of inflammatory diseases of the central nervous system.

In relation to the groups of patients aged 18 to 70 years under study, high accuracy indicators for predicting the severity of the course and outcome of viral encephalitis were obtained. False negative parameters in the formation of negative forecasts of encephalitis according to this formula were recorded at an insignificant level, as well as the level of error in the forecasts of successful outcomes. This indicates the prominent practical effectiveness of the presented multifactorial mathematical model and the expediency of using such mathematical models in the future in medical institutions. Therewith, all possible differences in predicting the outcomes of inflammatory diseases should be considered, since changes in the duration of neurometabolic therapy depend on this. Furthermore, it was found that reducing the planned duration of parenteral administration of drugs allowed considerably increasing the period of neurometabolic therapy in outpatient settings, which significantly reduces the time of therapy for hospitalized patients with inflammatory diseases of the central nervous system staying, at least up to several weeks.

The prospects for further scientific research in the direction determined by the subject of this study consist in the practical expediency of investigating the optimal possibilities of using a multifactorial mathematical model for predicting the severity of the course and outcomes of viral encephalitis in the practice of modern medical institutions.

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